REMARKS

Claims 34 and 40 have been amended to specify that the encoded protein is non-native to the secondary metabolic pathway of the plant, and also that the plant is of a type used as an animal feed, with the proviso that the plant is not rice or *Arabidopsis*. Support for the first amendment is found in e.g. claim 39 of record. Support for the latter amendment is found throughout the specification e.g. at page 18, line 16 to page 19, line 21.

Claims 39 and 47 have been cancelled.

Claim 49 has been amended in the same manner as claims 34 and 40.

Claims 49-66 have been amended to remove the limitation that the plant is a cruciferous plant, which was added by way of the amendment November 7, 2001 (paper No. 16). The genus *Oryza* has been deleted from claim 63.

New claims 67-80 have been added. Claims 67-76 are directed to embodiments of the invention wherein the plant is of the genus *Brassica*. These new claims find support in the specification at e.g. page 68 line 5 to page 73 line 27. Claims 77-80 specify particular plant families, genera, and crop species. Support is found in the original claims, and in the specification at e.g. page 31, lines 12-16, and page 56, lines 27-29.

A marked up copy of the amended claims, showing the changes made, and captioned "Version with markings to show Changes Made", is attached hereto.

Concerning 35 USC § 112

Claims 49-66 stand rejected under 35 USC 112, second paragraph as being indefinite over the recitation of "cruciferous" on the basis that the meaning of this phrase is unclear in light of the dependent claims. This rejection is rendered moot by the present amendment of claims 49-66 to delete reference to the expression "cruciferous".

Concerning 35 USC § 102

Claims 34-36, 39, 40-42, 44, 47, 48, 49, 50, 54, 55, 56, 58, 59, 60, 61, 62, 63 and 66 stand rejected under 35 USC 102(b) as being anticipated by Murata (EP 0 818 138 A1). The Examiner acknowledges that the methods taught by Murata are specifically directed to producing osmo-tolerant plants, but states that these methods inherently meet the limitations of the claims of record. The Examiner states that the transgenic plants recovered by Murata inherently have an altered nutritional profile by virtue of the fact that they express choline oxidase, and that these plants would have lower lignin and sinapine content.

Applicants respectfully submits that the claims, as presently amended, patentably distinguish from Murata. Independent claims 34, 40, and 49, as presently amended, specify that the plant is of a type used as an animal feed, with the proviso that said plant is not rice or *Arabidopsis*. Murata discloses only transformation of *Arabidopsis thaliana* and rice with a gene encoding choline oxidase. Murata provides no enabling support for transformation of plants used as animal feed, other than rice, as presently claimed.

Claims 34-37, 39, 44, 47-48 stand rejected under 35 USC 102(e) as being anticipated by Cheng *et al.* (U.S. Patent No. 5,948,667). The Examiner contends that the methods taught by Cheng *et al.* comprise the transformation of *Brassica napus* with an expression vector comprising a seed specific promoter (the oleosin promoter) and a coding sequence xylanase. The Examiner further contends that the transformation of the plant with a coding sequence for xylanase results in the production of transgenic plants with altered nutritional profiles because they contain a higher level of xylanase than wild type plants.

Applicants respectfully submit that Cheng does not anticipate the invention as presently proposed for amendment because Cheng does not expressly or inherently describe each and every element as set forth in the claims. More specifically, Applicants believe that Cheng does not describe the method steps of each rejected independent claim which essentially recite "selecting a nucleic acid sequence for its

ability to encode a protein capable of modifying the utilization of a substrate in [a secondary metabolic pathway] associated with a nutritional profile of a plant, said protein being non-native to said [secondary metabolic pathway]." In this regard, Applicants respectfully submit that the Examiner has not shown that the recombinant xylanase enzyme described by Cheng would modify the utilization of a substrate in any known secondary metabolic pathway of a plant. Rather than modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, Applicants submit that the xylanase enzyme described by Cheng is described to act upon xylan components in hemicellulose, a final product found in plant primary and secondary cell walls. Furthermore, the transgenic *Brassica* example cited by the Examiner (Example 5.C.ii.) teaches an oleosin-xylanase fusion wherein the xylanase is rendered stable in an "immobilized enzyme matrix" until the resulting transgenic oil-bodies are crushed. (Cheng, col. 18, lines 16-67). Applicants thus submit Cheng's methods are inapposite with the present invention in that Cheng expressly teaches rendering xylanase unavailable (by immobilization) for use in any secondary metabolic pathway. As Cheng merely describes production of xylanase as an industrial enzyme in Brassica, and not modifying the nutritional profile of a plant by modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of the plant, Applicants respectfully request the amendment be entered and the rejections be withdrawn.

Claims 34-36, 39, 44, 46, 47 and 48 stand rejected under 35 USC 102(b) as being anticipated by Chapple *et al.* (WO 97/23599), and claims 40, 48, 49-51, 54, 58, 59, 60, 61, 62, 63, 64, 65 and 66 stand rejected under 35 USC 102(a) as being anticipated by Chapple *et al.* The Examiner states that Chapple *et al.* teach the transformation of plants with the F5H gene in order to alter the lignin content in plants and that Chapple *et al.* exemplify this method in the transformation of *Arabidopsis thaliana* (a crucifer) and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (*Brassica*) (page 7, lines 15-20). The Examiner states that since the F5H gene effects the production of a product in the phenylpropanoid pathway which is necessary for the production of sinapine (i.e. 5-hydroxyferulic

acid), plants with decreased F5H activity as taught by Chapple *et al.* would inherently have the property of decreased sinapine levels compared to the wild-type plants.

Applicants respectfully submit that the presently amended claims patentably distinguish from Chapple *et al.* Independent claims 34, 40 and 49 have been amended to specify that the nucleic acid sequence introduced into the plant encodes a protein that is non-native to the secondary metabolic pathway. In contrast, Chapple *et al.* transforms the plant with a gene encoding a protein that is native to the secondary metabolic pathway. Chapple *et al.* transformed *Arabidopsis* plants with a gene encoding the F5H enzyme. But as shown in Figure 1 of Chapple *et al.*, the F5H enzyme is native to the plant metabolic pathway for lignin synthesis. Chapple *et al.* does not teach or suggest transforming a plant with a protein that is non-native to the secondary metabolic pathway of interest, as presently claimed.

Claims 34, 35, 36, 39, 40, 46, 47, 48, 49, 50, 51, 54, 58, 59, 60, 61, 62, 63, 64, 65 and 66 of record stand rejected under 35 USC 102(b) as being anticipated by Van Doorsselaere *et al.* (WO 93/05160). The Examiner states that Van Doorsselaere *et al.* teach the transformation of plants with a nucleic acid encoding O-methyl transferase (OMT) in order to alter the lignin content in plants. The Examiner states that Van Doorsselaere *et al.* exemplify this method in transformation of poplar trees and further teach that this method is useful to transform other plants such as alfalfa, rice, maize and oil seed rape (*Brassica*) (page 13, lines 15-26). The Examiner contends that the OMT gene effects the production of a product in the phenylpropanoid pathway that is necessary for the production of sinapine (i.e. ferulic acid), and therefore plants with decreased OMT activity as taught by Van Doorsselaere *et al.* would inherently have the property of decreased sinapine levels compared to the wild-type plants.

Applicants respectfully submit that the presently amended claims patentably distinguish from Van Doorsselaere *et al.* As discussed above, independent claims 34, 40 and 49 have been amended to specify:

(1) that the plant is of a type used as an animal feed, with the proviso that the plant is not rice; and

(2) that the nucleic acid sequence encodes a protein that is non-native to the secondary metabolic pathway.

Van Doorsselaere *et al.* do not teach or suggest either of these limitations in Applicants' claims. Van Doorsselaere *et al.* only exemplify the transformation of poplar trees with a nucleic acid molecule encoding poplar OMT (see Van Doorsselaere *et al.*, page 19, line 26 to page 20, line 14). Hence Van Doorsselaere *et al.* used an OMT sequence native to the poplar lignin biosynthetic pathway. Thus Van Doorsselaere *et al.* fail to teach or suggest use of a nucleic acid sequence encoding a protein non-native to the secondary metabolic pathway of the plant. Secondly, poplar clearly is not a plant of a type used as an animal feed, as presently claimed.

Van Doorsselaere *et al.* mention at page 13, lines 15-26 that their methods would be useful to transform other plants such as alfalfa, rice, maize, and oil seed rape, but provide no enabling details of how this would be accomplished or any evidence that any of such plants would have an altered or improved nutritional profile as specified in the instant claims. In contrast, Applicants provide working examples of *Brassica napus* (i.e. alfalfa - an animal feed crop) with nucleic acid sequence encoding choline oxidase (COX) resulting in reduced sinapine levels (i.e. improved nutritional profile) (see the instant specification in Examples 4 and 5 from page 68 to page 74).

Concerning 35 USC § 103

Claims 38 and 52 of record stand rejected under 35 USC 103(a) as being unpatentable over Murata in view of Willmitzer *et al.* (WO 92/01042).

The Examiner has rejected Applicants' previous arguments concerning the 103(a) rejection over Murata *et al.* in view of Willmitzer *et al.* The Examiner states that Murata *et al.* is relied upon for their teaching of the methodology for the expression of choline oxidase and transgenic plants, and that although Murata *et al.*'s purpose for completing such a method is different than the motivation provided in the rejection, nonetheless, Murata *et al.* provide a method for transforming plants of industrial

enzyme. The Examiner states that the teachings of Willmitzer *et al.* provide an alternate use for the methods of Murata *et al.* and provide a motivation to modify the method for transforming plants with choline oxidase. The Examiner concludes that the transformation of plants with choline oxidase using a seed-specific promoter provides a new use for methods which utilize plants transformed with choline oxidase as taught by Murata *et al.* (see the Office Action at the paragraph bridging pages 16 and 17).

Applicants respectfully traverse this rejection and submit that presently amended claims 38 and 52 patentably distinguish from Murata *et al.* in view of Willmitzer *et al.* The instant claims are directed to altering a nutritional profile of a plant by transforming the plant with a nucleic acid sequence encoding a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, the protein being non-native to the secondary metabolic pathway. By way of example, in an exemplified case, a choline oxidase gene is introduced into the plant to modify the utilization of a substrate in the phenylpropanoid pathway, resulting in reduced sinapine levels in the plant.

As discussed above and in Applicants' response of November 7, 2001, (paper No. 16), Murata *et al.* is concerned only with osmo-tolerance. There is no teaching or suggestion concerning altering a nutritional profile of the plant. In contrast, the teachings of Willmitzer *et al.* are not directed to improving the nutritional profile of a plant, but rather to the use of plants for the transgenic expression of industrial enzymes — i.e. "gene farming". Willmitzer *et al.* are very clear that it is not their purpose to change the physical characteristics of the plant itself, going so far as to state in the abstract that "A transgenic plant comprises an inserted DNA sequence encoding an industrial enzyme which is heterologous to said plant, with the exception of enzymes conferring improved growth properties or desirable physical characteristics to living plants producing them". This phrase is repeated in Willmitzer *et al.* at e.g. page 2, lines 23 to 28. Hence, Willmitzer *et al.* clearly teach away from the presently claimed invention, as Willmitzer *et al.* specify that the transgene should not affect the physical characteristics of the plant.

Willmitzer *et al.* are concerned with the production of heterologous industrial enzymes by plants, not with modifying the nutritional profile of the plant by modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of the plant. Applicants respectfully submit that the Examiner is improperly selecting short excerpts out of Willmitzer *et al.*, taken out of context. Applicants respectfully submit that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. See *W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F. 2d 1540, 220 USPQ 303 (Fed. Cir. 1983).* Taken as a whole, Willmitzer *et al.*, who specify that the heterologous enzymes should not confer improved growth properties or desirable physical characteristics on the plant producing the enzyme, clearly teach away from the presently claimed invention.

Claims 38 and 52 stand rejected under 35 USC 103(a) as being obvious over Chapple *et al.* (WO 97/23599) in view of Kennley *et al.* (WO 56/62958) and Willmitzer *et al.* (WO 92/01042).

Applicants respectfully traverse this rejection and submit that the claims, as presently amended, patentably distinguish from Chapple *et al.* in view of Kennley *et al.* and Willmitzer *et al.* As discussed above, Chapple *et al.* teach the transformation of *Arabidopsis thaliana* with the F5H gene in order to alter the lignin content of the plant. The F5H gene is native to the phenylpropanoid secondary metabolic pathway. The presently amended claims specify that the nucleic acid sequence inserted into the plant encodes a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, said protein being non-native to said secondary metabolic pathway. Chapple *et al.* do not teach or suggest that the encoded protein is non-native to the secondary metabolic pathway, and this deficiency in the reference is not cured by either Kennley *et al.* or Willmitzer *et al.*

Claim 45 stands rejected under 35 USC 103(a) as being unpatentable over Van Doorsselaere *et al.* in view of Chapple *et al.* (The Plant Cell, Vol. 4, 1413-1424). Applicants respectfully traverse this rejection and submit that claim 45, as presently

amended, patentably distinguishes from Van Doorsselaere *et al.* in view of Chapple *et al.* Claim 40 from which claim 45 depends, has been amended to specify that:

(1) the plant is of a type used as an animal feed other than rice; and

(2) the nucleic acid sequence encodes a protein that is non-native to the phenylpropanoid pathway.

As discussed above, Van Doorsselaere *et al.* exemplify transformation only of poplar trees with the OMT gene to modulate lignin composition. Poplar trees are not an animal feed plant, as required by the instant claims. Van Doorsselaere *et al.* mention that the described methods could be used in other plants, but do not provide any description of how this would be accomplished or that there would be any reasonable expectation of success in modulating lignin composition by such a method. Chapple *et al.* state, at the end of the second column on page 1420 that the introduction or alteration of expression of ferulate-5-hydroxylase (F5H) may be an important factor in modifying lignification in economically important plants. That modulating F5H expression can modify lignin content might be "worth a try" would not lead a person of ordinary skill in the art to believe that such a result could be achieved with any reasonable expectation of success.

Secondly, neither Van Doorsselaere *et al.* nor Chapple *et al.* suggest use of a nucleic acid encoding a protein that is non-native to the phenylpropanoid pathway, as presently claimed. As shown in Figure 1 of the Chapple *et al.* reference, both the OMT enzyme taught by Van Doorsselaere *et al.* and the F5H enzyme taught by Chapple *et al.* are native to the phenylpropanoid pathway. Neither reference teaches nor suggests use of a nucleic acid encoding a protein non-native to the phenylpropanoid pathway, as presently claimed.

Concerning the Examiner's Response to Applicants' Remarks

Although Applicants believe the 102 rejections of the claims over Murata *et al.* are rendered moot by the instant amendments to specify that the plant is of a type used as an animal feed other than rice, Applicants respectfully traverse the Examiner's conclusion that the methods of Murata *et al.* inherently meet the method steps of the claims of record. The Examiner contends that the fact that Murata *et al.* intend their method for different purposes immaterial to the fact that their method anticipates Applicants' claimed method. The Examiner contends that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. The Examiner contends that, in a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art; in the instant case, the method taught by Murata *et al.* is no different from the instantly claimed nucleic acid molecules. Since it is the transformation of the plants of choline oxidase that causes the change in the nutritional profile of the plants, the plants produced using the methods taught by Murata *et al.* would inherently have an altered nutritional profile.

Applicants respectfully disagree. Claim 34 of record positively recites the step of selecting a nucleic acid sequence for its ability to encode a protein capable of modifying utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant. Murata *et al.*, who were only concerned with osmo-tolerance, do not teach or suggest this positive selection step. Applicants respectfully submit that weight must be given to all claim limitations. Claim 34 does not merely include transformation in recovery steps, but also includes the above-mentioned positive selection step. Even if the transformed plants of Murata *et al.* inherently have an altered nutritional profile (of which there is no evidence) the positive selection step of the instant claims is not inherent to Murata *et al.*

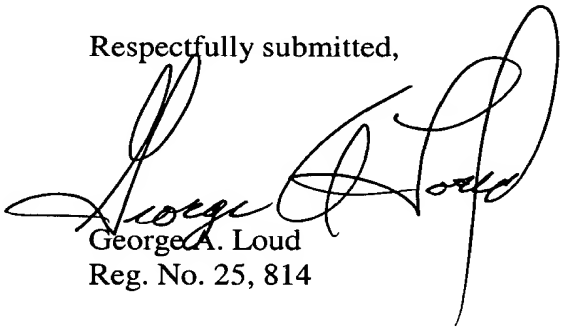
Concerning Allowable Subject Matter

Applicants acknowledge the Examiner's findings that claims 43 and 57 of record are directed to patentable subject matter.

In view of all the foregoing, entry of the amendments and further consideration of this application, leading to its timely allowance, are respectfully requested.

If it is believed that a telephone conference with Applicants' agent would expedite the prosecution of this application, the Examiner is requested to call the undersigned at the below-identified telephone number.

Respectfully submitted,



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Version With Markings To Show Changes Made

34. (Once amended) A method for altering a nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of a substrate in a secondary metabolic pathway associated with a nutritional profile of a plant, said protein being non-native to said secondary metabolic pathway;

transforming a plant cell of said plant with an expression cassette comprising said nucleic acid sequence, said plant being of a type used as an animal feed, with the proviso that said plant is not rice or *Arabidopsis*; and

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant.

Claim 39 has been cancelled.

40. (Once amended) A method for altering a nutritional profile of a plant, comprising the steps of:

selecting a nucleic acid sequence for its ability to encode a protein capable of modifying the utilization of a substrate in the phenylpropanoid pathway of said plant, said protein being non-native to said phenylpropanoid pathway;

transforming a plant cell of said plant with an expression cassette comprising said nucleic acid sequence, said plant being of a type used as an animal feed, with the proviso that said plant is not rice or *Arabidopsis*; and

recovering a genetically altered plant from said plant cell, said genetically altered plant characterized by an altered nutritional profile relative to a wild-type of said plant.

Claim 47 has been cancelled.

49. (Once amended) A genetically modified [cruciferous] plant or a descendant thereof, said plant being of a type used as an animal feed, with the proviso that said plant is not rice or *Arabidopsis*, said plant comprising a recombinant nucleic acid sequence stably incorporated into the genome of said plant, said recombinant nucleic acid sequence encoding a protein which modifies the utilization of a substrate in the phenylpropanoid metabolic pathway of said plant, said protein being non-native to said phenylpropanoid metabolic pathway, said plant having an improved nutritional profile relative to a wild-type of said plant.

50. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said substrate is not a primary metabolite of the group selected from glucose, amino acids, common fatty acids and nucleotides.

51. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said nucleic acid sequence is under the control of a tissue selective promoter.

52. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 51, wherein said promoter is seed selective.

53. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 52, wherein said seed selective promoter is a phaseolin promoter or a napin promoter.

54. (Once amended) A plant cell, plant seed, plant component or plant progeny derived from the genetically modified [cruciferous] plant of claim 49.

55. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said encoded protein is a choline metabolizing enzyme.

56. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 55, wherein said choline metabolizing enzyme is choline oxidase.

57. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 56, wherein said nucleic acid sequence encoding said choline oxidase is under the control of a seed-selective promoter active in plant cells, and wherein said expression cassette further comprises a nucleic acid sequence that encodes a betaine aldehyde dehydrogenase capable of converting betaine aldehyde to betaine, said betaine aldehyde dehydrogenase encoding nucleic acid sequence being under the control of a seed-selective promoter active in plant cells.

58. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said improved nutritional profile comprises an altered lignin content relative to said wild-type of said plant.

59. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said improved nutritional profile comprises a reduced sinapine content relative to said wild-type of said plant.

60. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said plant is a member of the Dicotyledoneae or Monocotyledoneae.

61. (Once amended) The genetically modified[cruciferous] plant or descendant thereof of claim 49, wherein said plant is a member of a family selected from the group consisting of Malvaceae, Linaceae, Compositae, Fabaceae, Euphorbiaceae, Gramineae and Oleaceae.

62. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said plant is a member of the family Brassicaceae (= Cruciferae).

63. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said plant is a member of a genus selected from the group consisting of *Linum, Gossypium, Glycine, Arachis, Carthamus, Helianthus, Medicago, Sinapis, Raphanus, Ricinus, Olea, Zea, Hordium,* and *Triticale*[, and *Oryza*].

64. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said plant is of the genus *Brassica*.

65. (Once amended) The genetically modified [cruciferous] plant or descendant thereof of claim 49, wherein said plant is *Brassica napus* or *Brassica rapa*.

66. (Once amended) An animal feed derived at least in part from the genetically modified [cruciferous] plant or descendant thereof of claim 49.

Claims 67-80 are new.